ADHD in the mainstream: the role of emotional dysregulation and overlap with common mental health disorders

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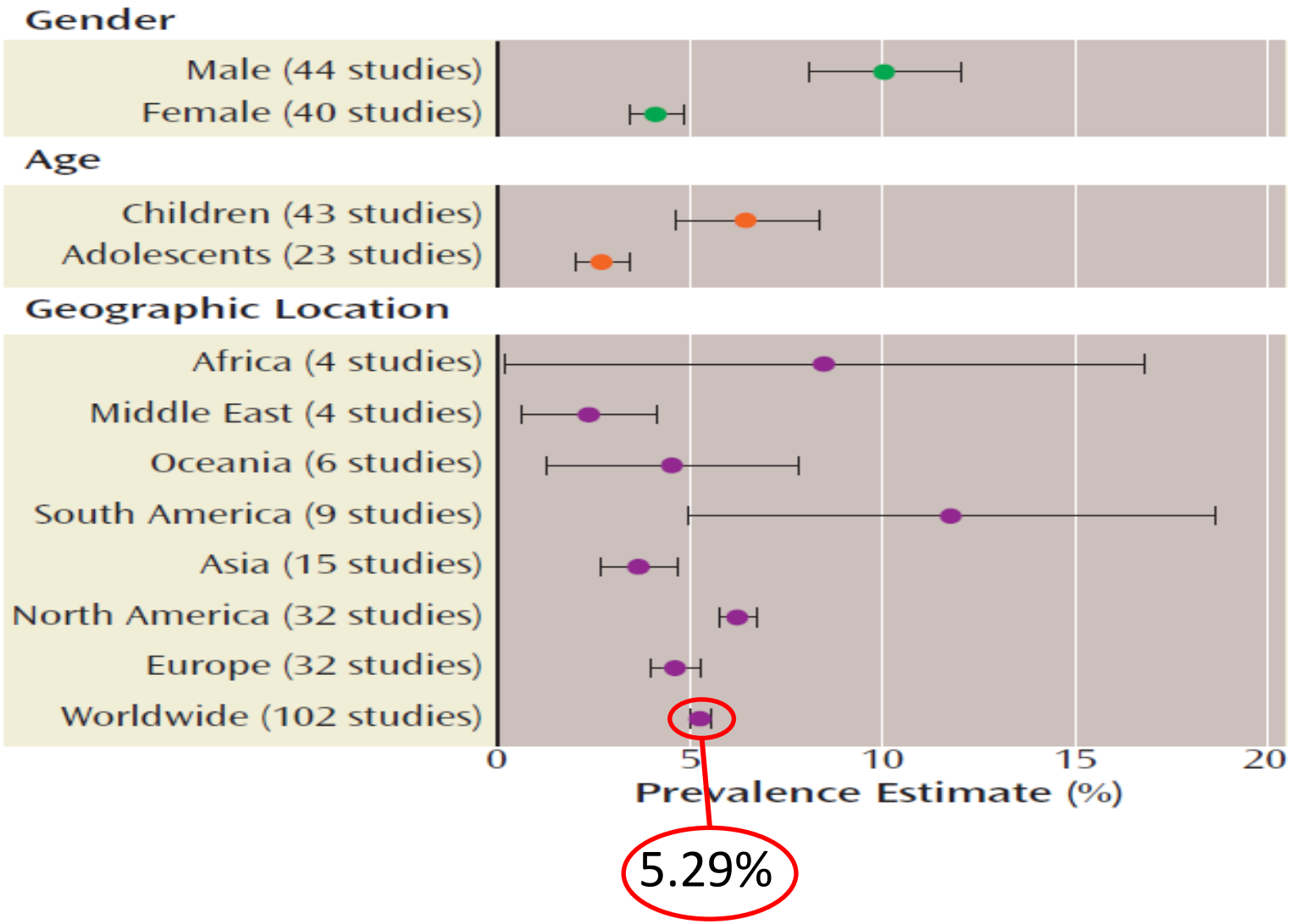
MRC Social Genetic and Developmental Psychiatry

The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007– 2013) under grant agreement n° 602805

ADHD in the mainstream

- Neurodevelopmental disorder
  - early onset
  - late onset
- Neurodiversity
- Mental health disorder (medical treatment)
- Learning Difficulty

Population prevalence rates



Polanczyk et al 2007

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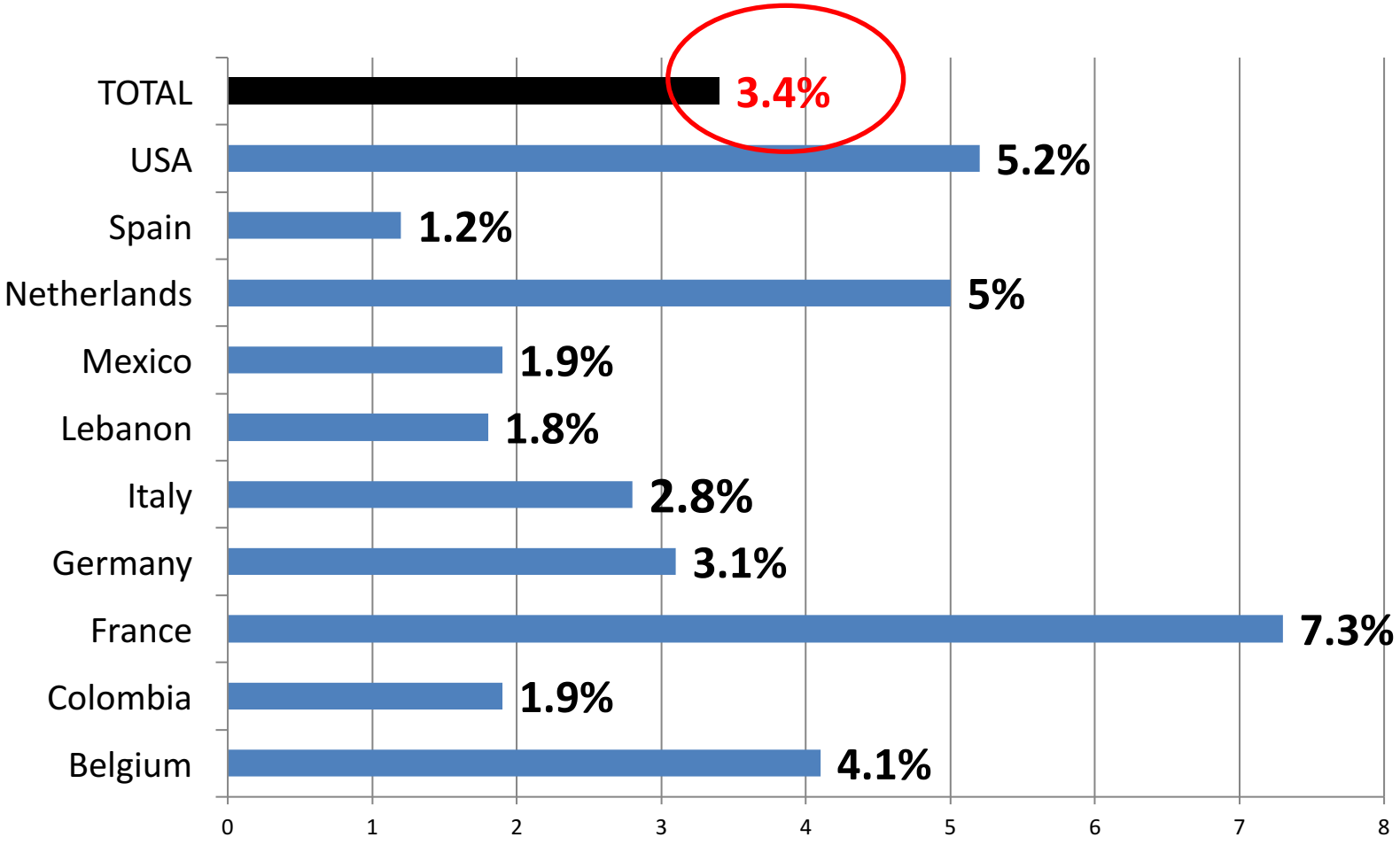
Prevalence of adult ADHD



Fayyad et al., Br J Psychiatry. 2007 May;190:402-9.

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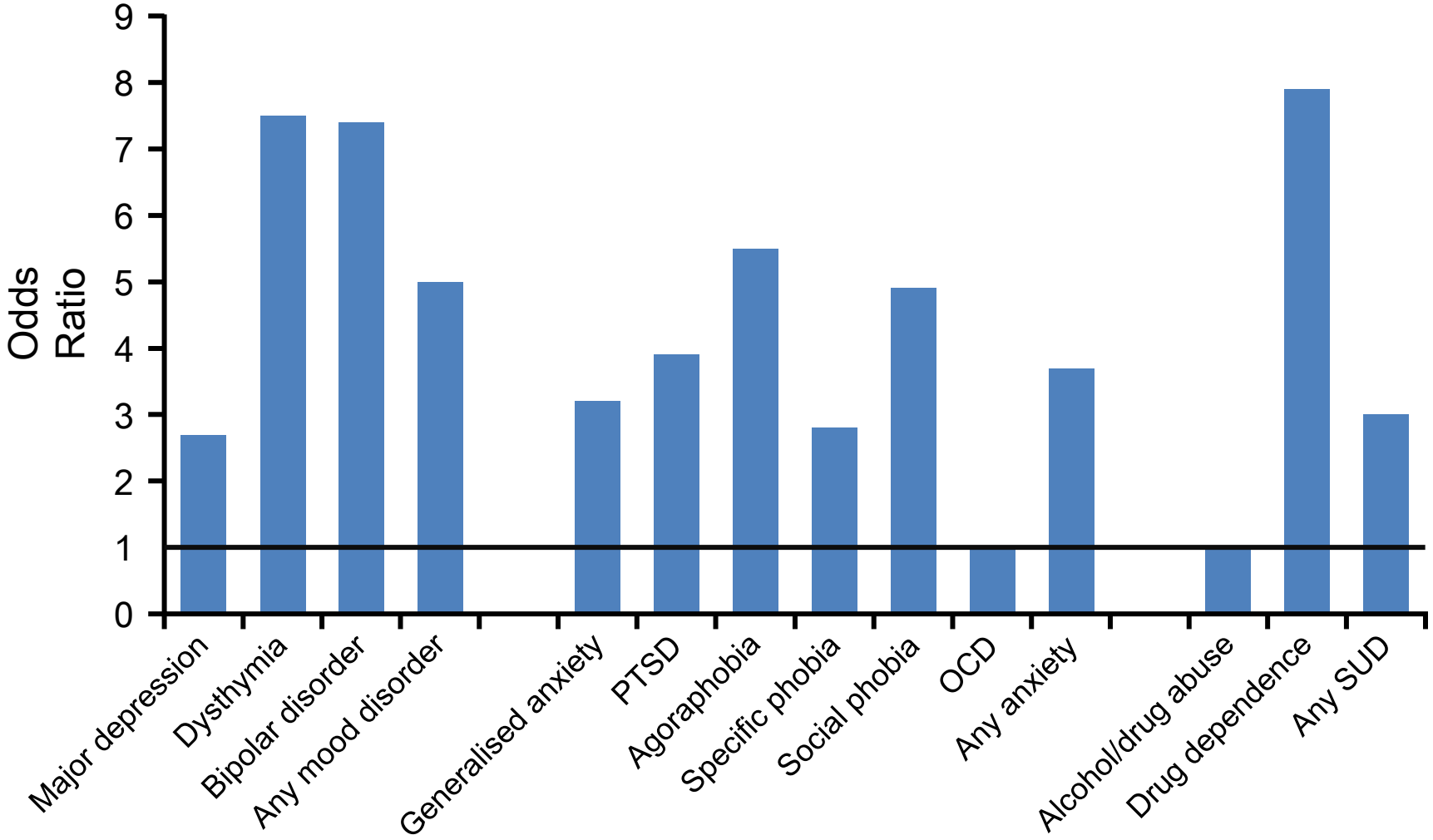
Risks of co-occurring disorders

(US national co-morbidity survey)



Kessler RC, et al. Am J Psychiatry 2006; 163:716—23.

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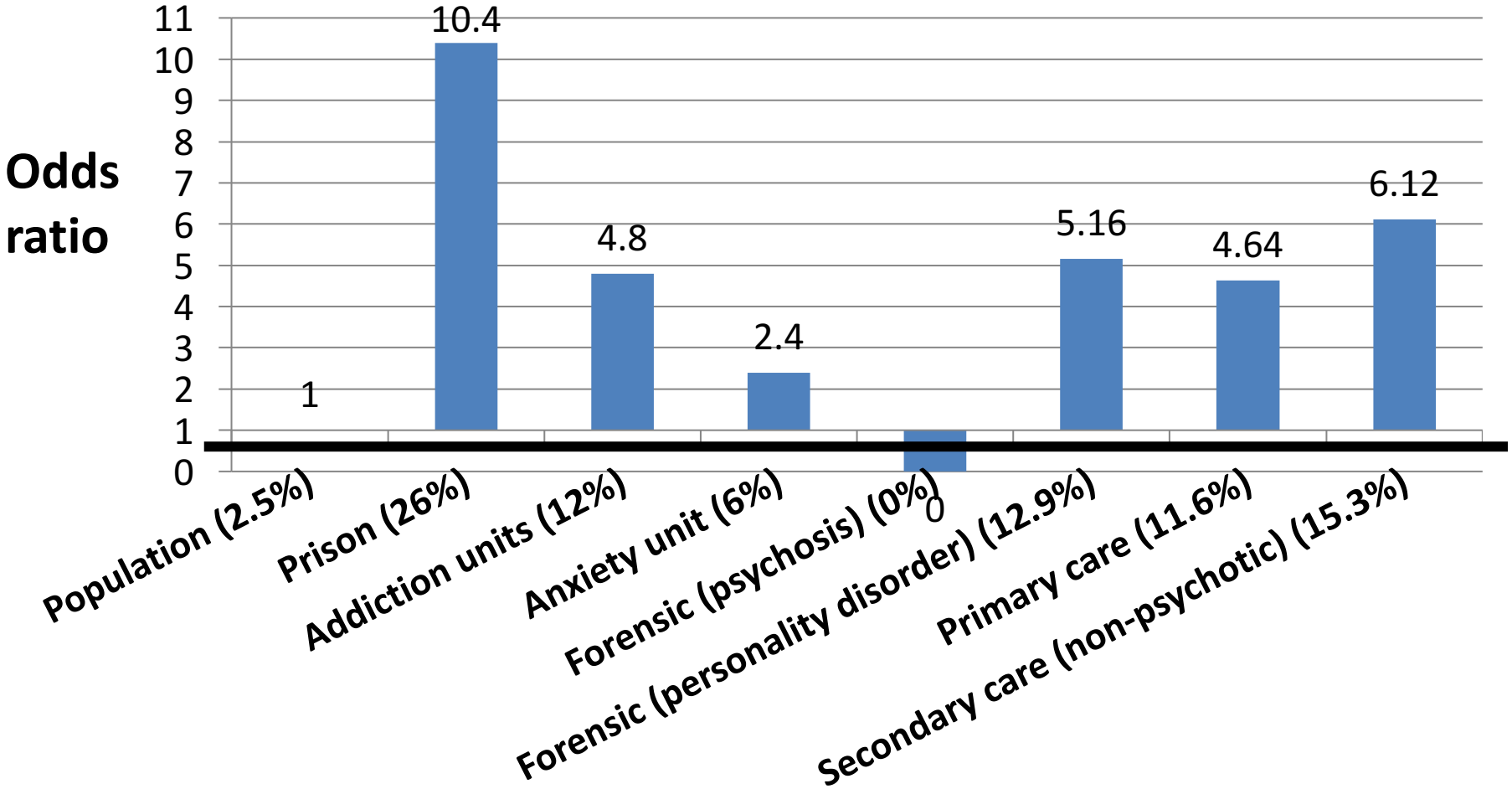
Rates of ADHD within adult mental health services



Murphy et al., NIHR report, 2013; Deberdt et al., BMC Psychiatry, 2015;

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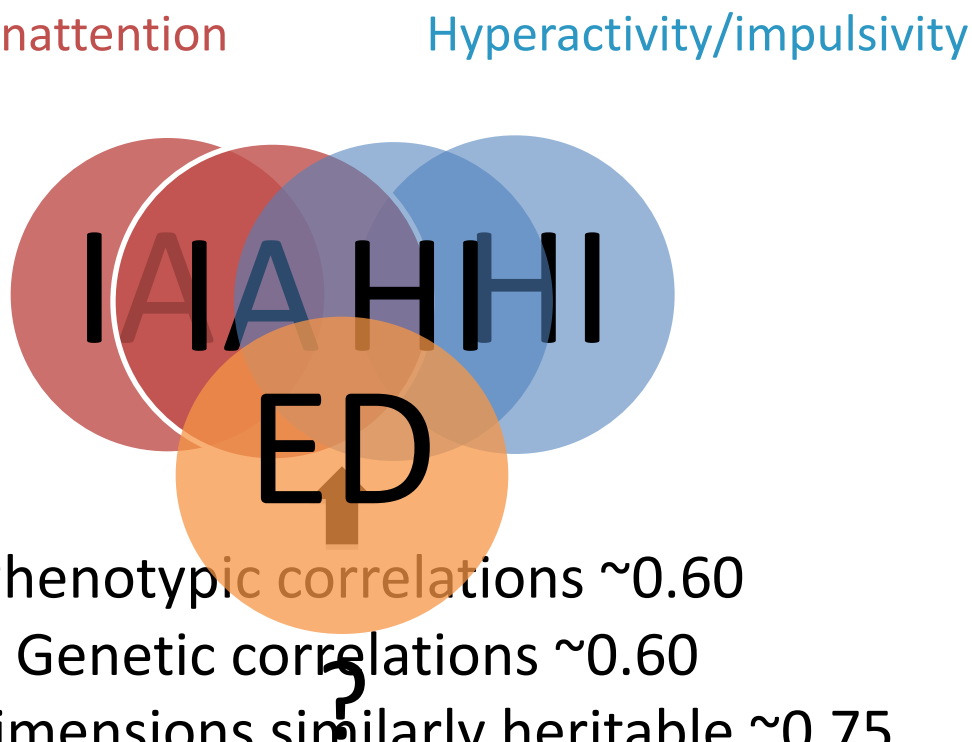
ADHD characterised by two or more symptom domains

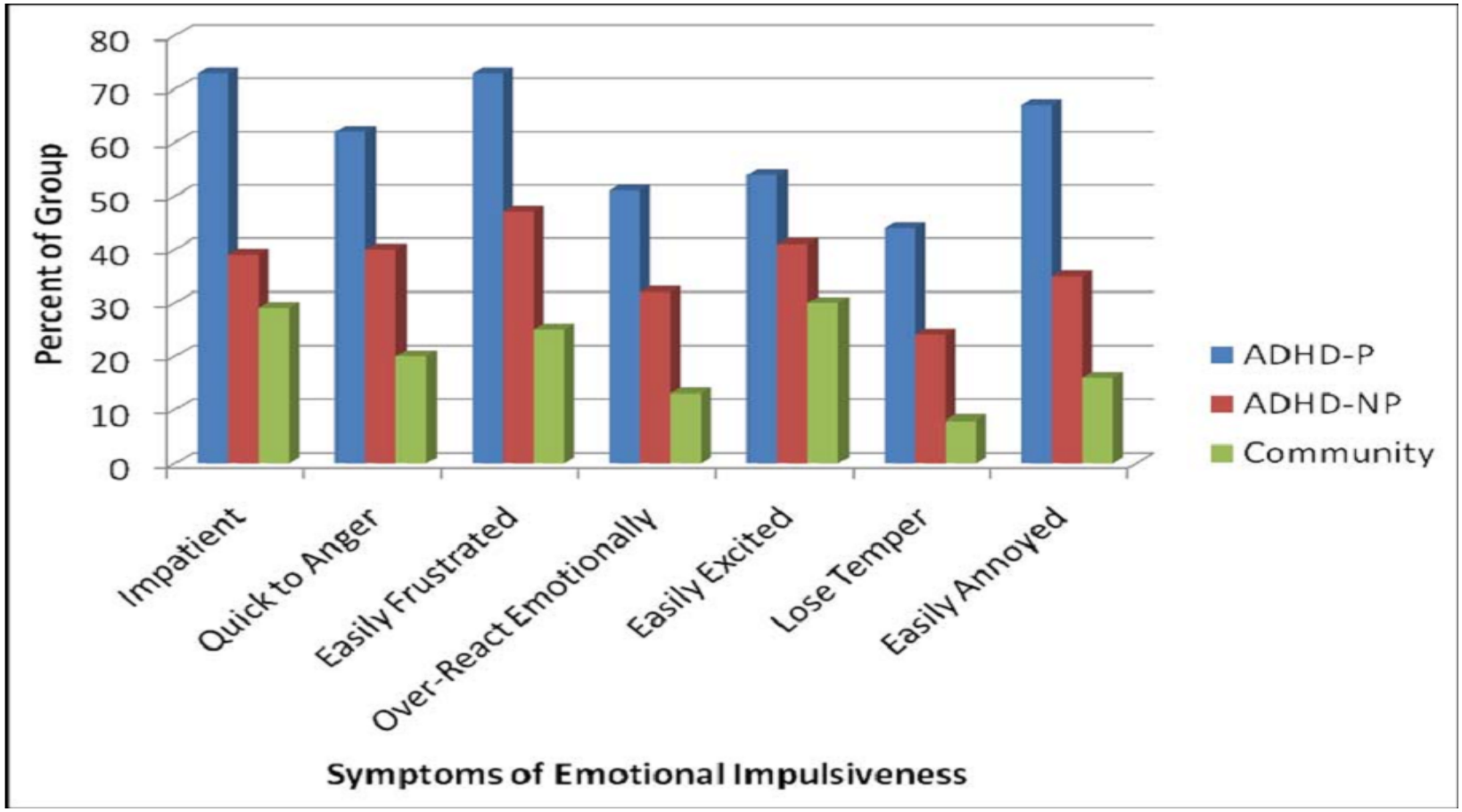


Phenotypic correlations ~0.60

Genetic correlations ~0.60

Both dimensions similarly heritable ~0.75

Symptoms of Emotional Impulsiveness in an adult follow-up (mean = age 27) sample of children with ADHD and community controls



Barkley and Fischer, JAACAP, 2010

The unique contribution of Emotional Impulsiveness to psychosocial impairments

Severity of Emotional Instability uniquely contributed to numerous impairments:

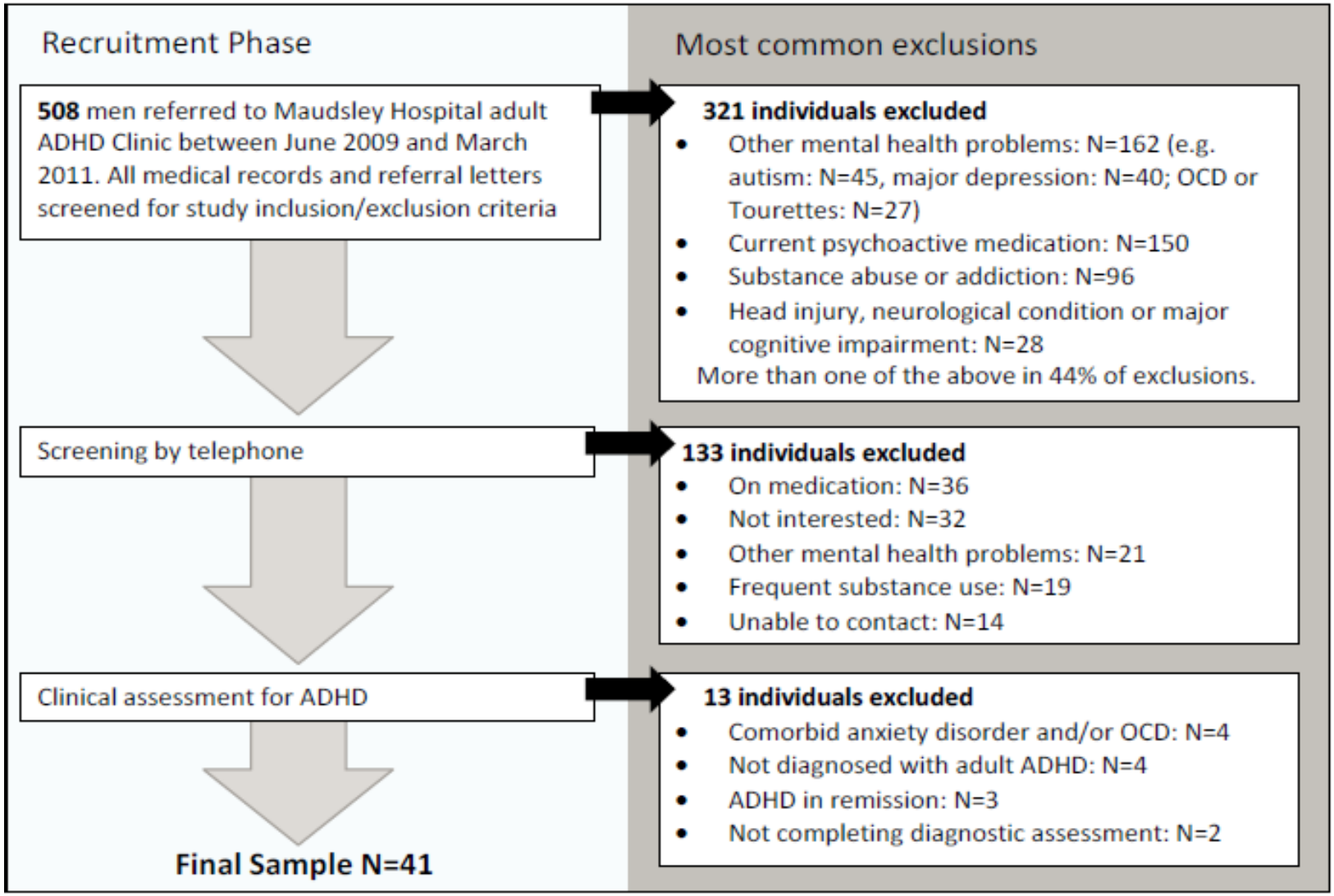
- Home life
- Occupation
- Education
- Criminal Activity
- Driving
- Financial outcomes

"EI is as much a component of ADHD as the two traditional dimensions"

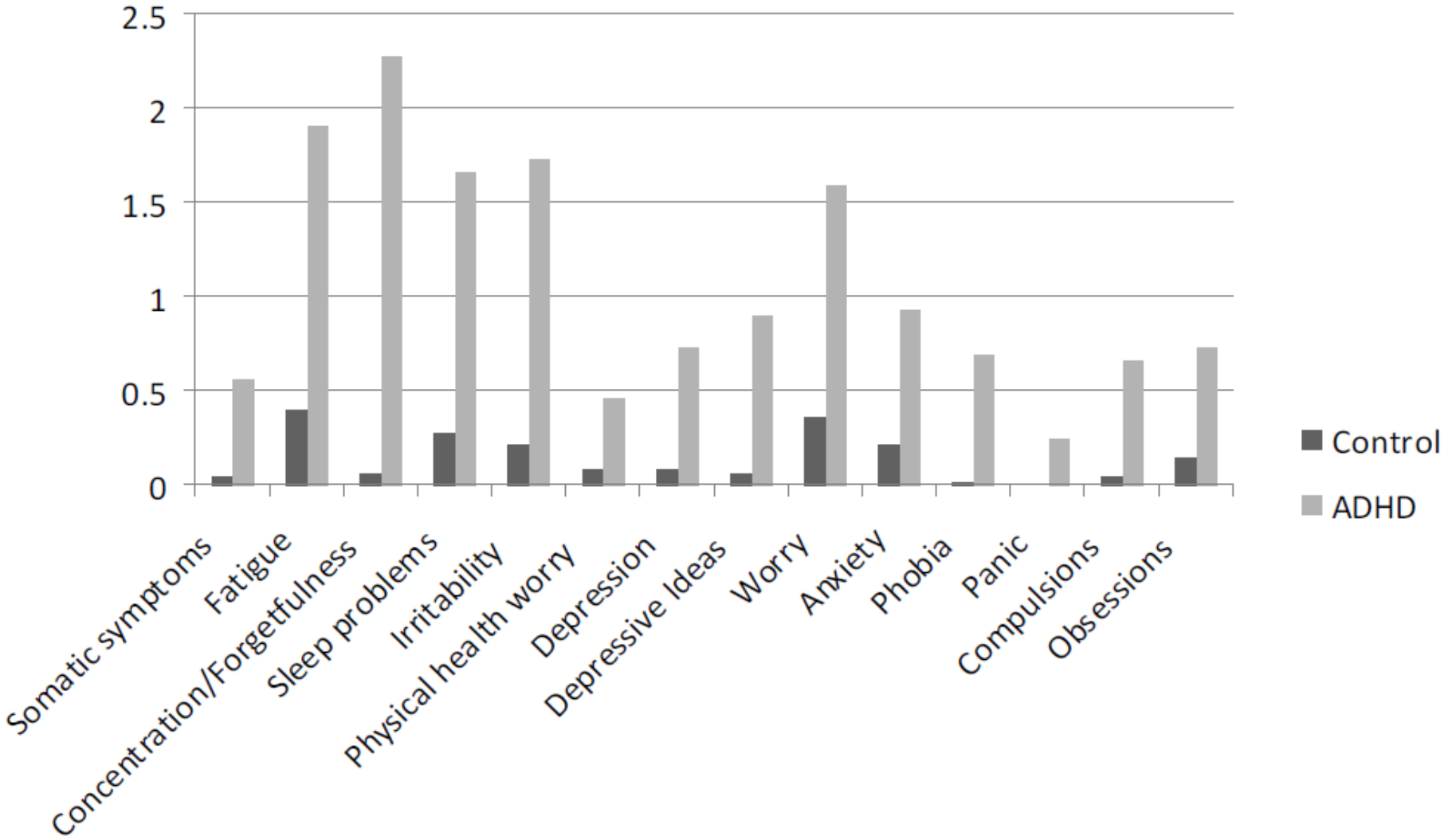
Barkley and Fischer, JAACAP, 2010

MIRIAD project

Highly selected sample with no comorbidity and medication free



Sub-threshold psychopathology in ADHD



Skirrow & Asherson 2012

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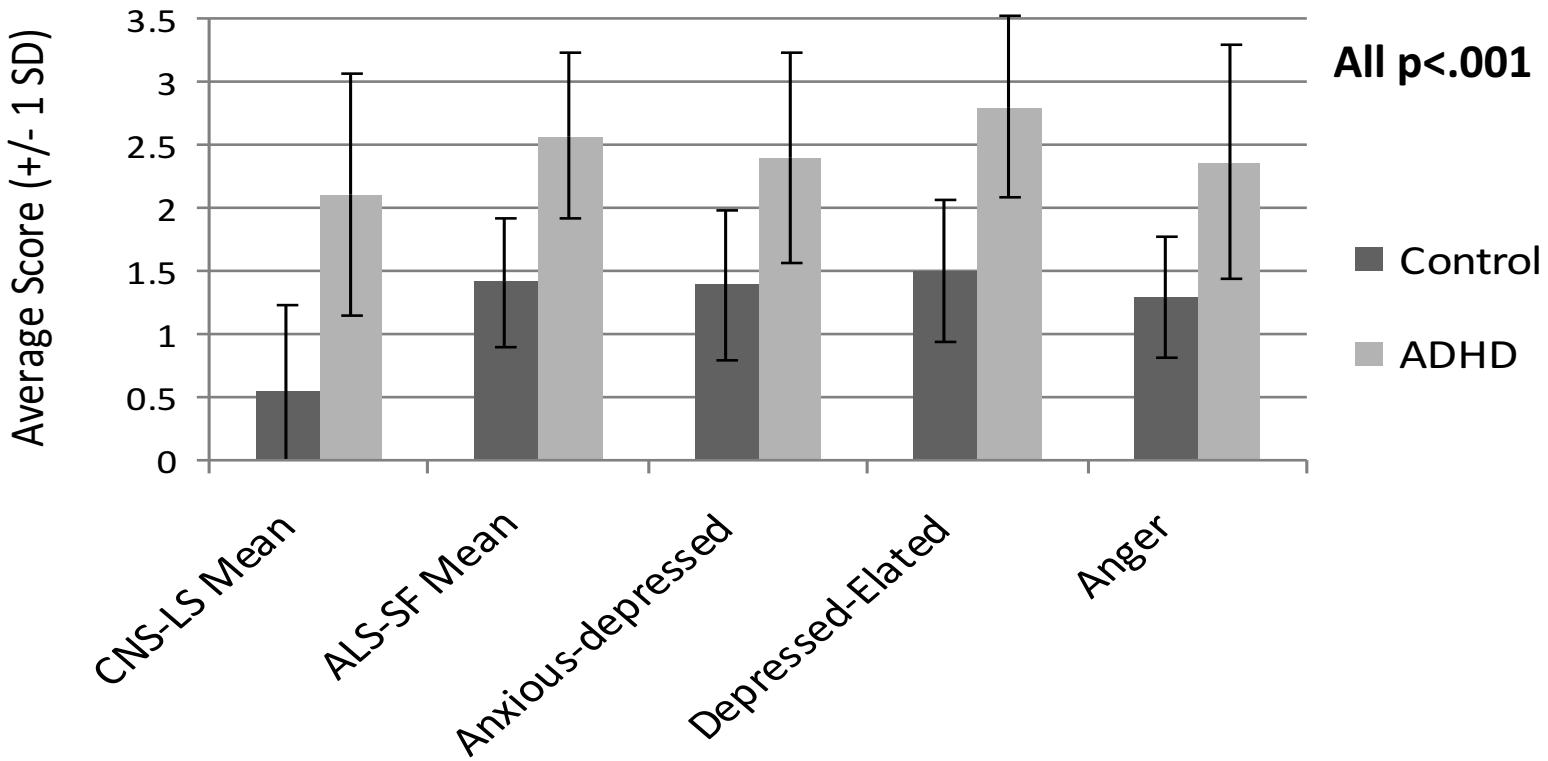
Case-control differences for emotional lability scores



ADHD	Sensitivity	Specificity
CNS-Lability scale (CNS-LS)	.88	.83
Affective lability scale (ALS)	.85	.81

Skirrow & Asherson JAD, 2013

Predictors of functional impairment in adults with ADHD

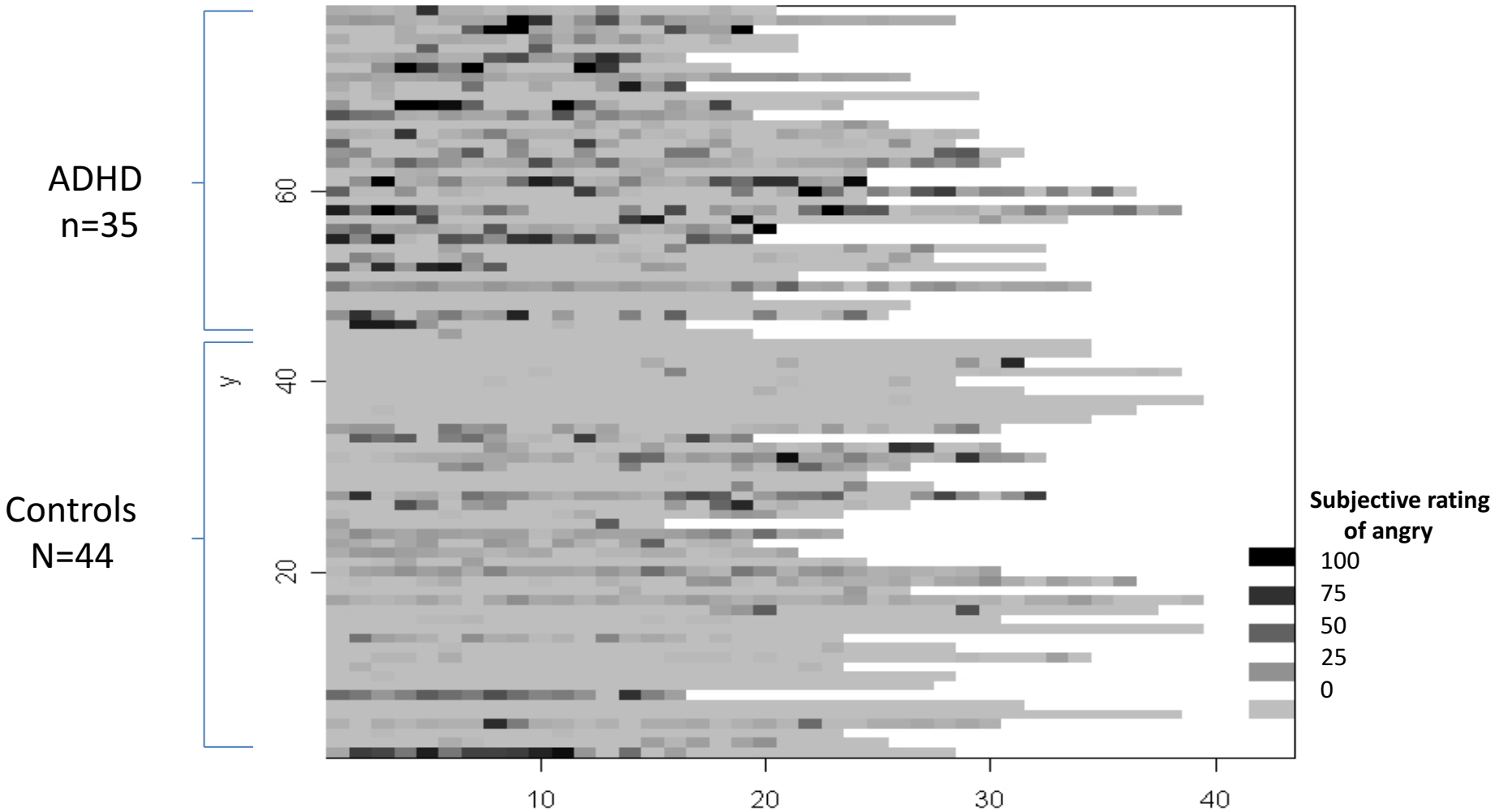
Impairment/predictors	Beta	R	R^2	p
Family				
Emotional lability (CNS-LS)	.59	.59	.35	<.001
Education				
Emotional lability (CNS-LS)	.44	.44	.19	.013
Life Skills				
Emotional lability (CNS-LS)	.61	.61	.38	<.001
Self concept				
Comorbid symptoms (CIS-R)	.55	.55	.30	<.001
Social problems				
Emotional lability (CNS-LS)	.35	.56	.32	<.001
Hyperactivity-impulsivity (BRS)	.35	.68	.40	<.001
Risk (inverse transformed)				
Hyperactivity-impulsivity (BRS)	-.48	.48	.23	.001

Skirrow & Asherson, JAD, 2013

The Experience sampling method (ESM)

- Participant wears a watch which vibrates at varying intervals
- Then they fill out a questionnaire on the PDA
- Responses collected 8 times a day for a working week (mon-fri)

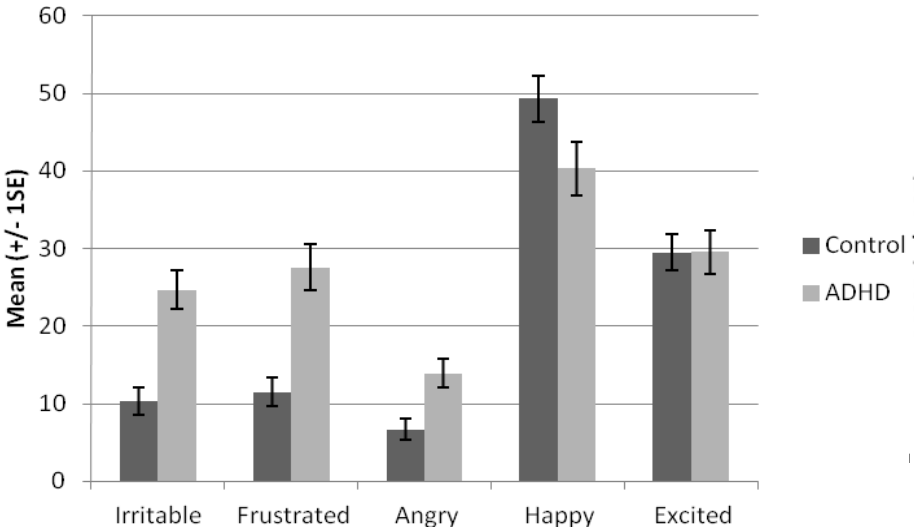
Anger ratings for individuals with ADHD and healthy controls over the 5-day period

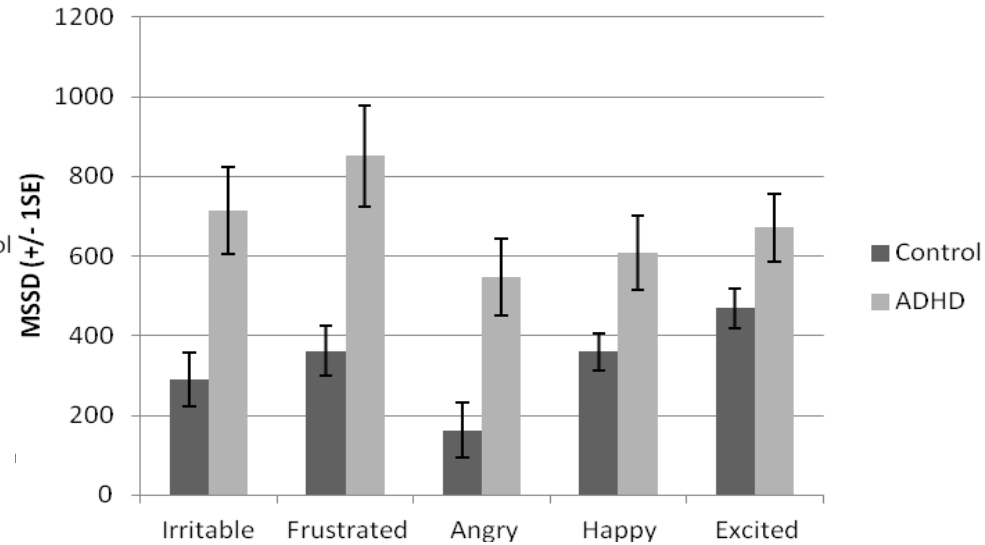


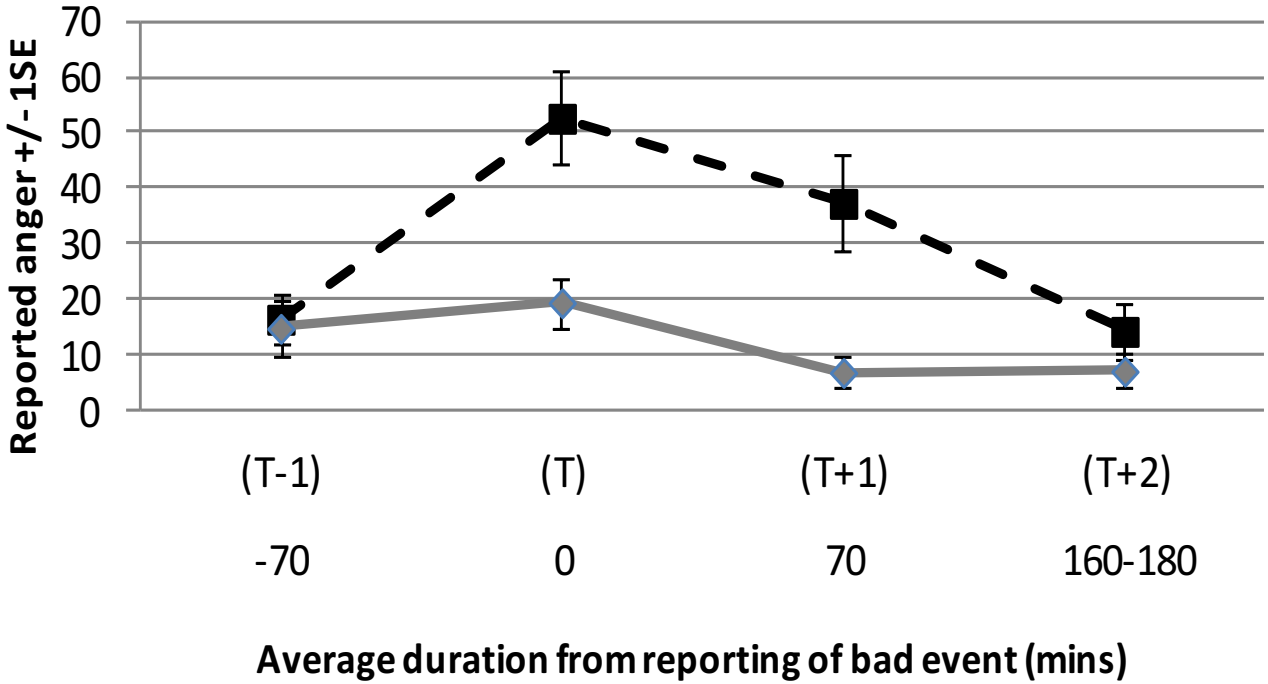
(Matched for age, IQ and years in education)

Adapted from Skirrow et al., Pschol Med, 2014; KCL PhD 2013

Experience sampling of emotional symptoms

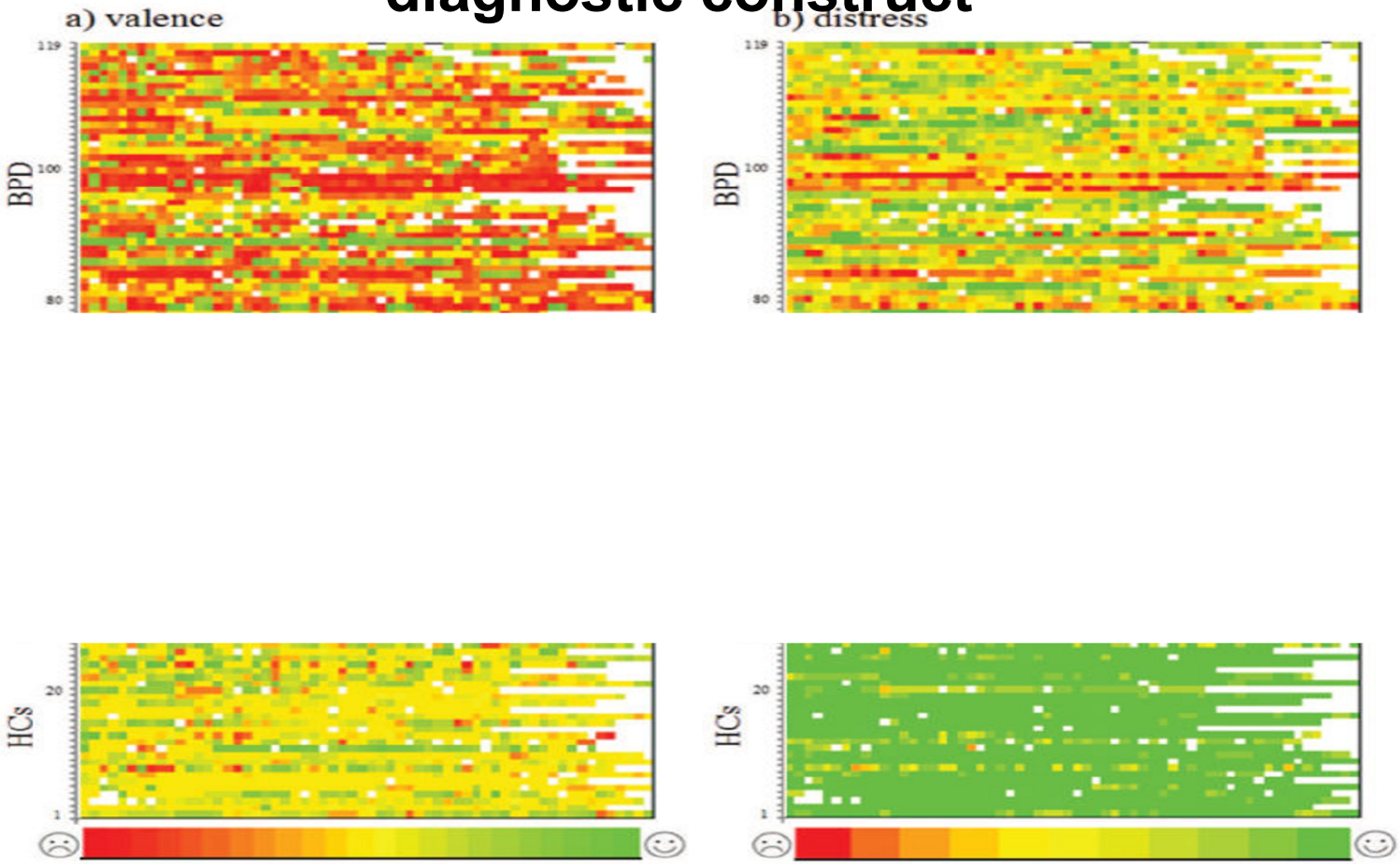






Skirrow et al., Pschol Med, 2014

Affective instability in borderline personality (BPD) disorder, post-traumatic stress disorder (PTSD), bulimia nervosa (BN) and healthy controls (HC): a trans-diagnostic construct



Ratings every 15 minutes during 24 hours.

Santangelo et al., J Abnorm Psychol, 2014, 123: 258-272

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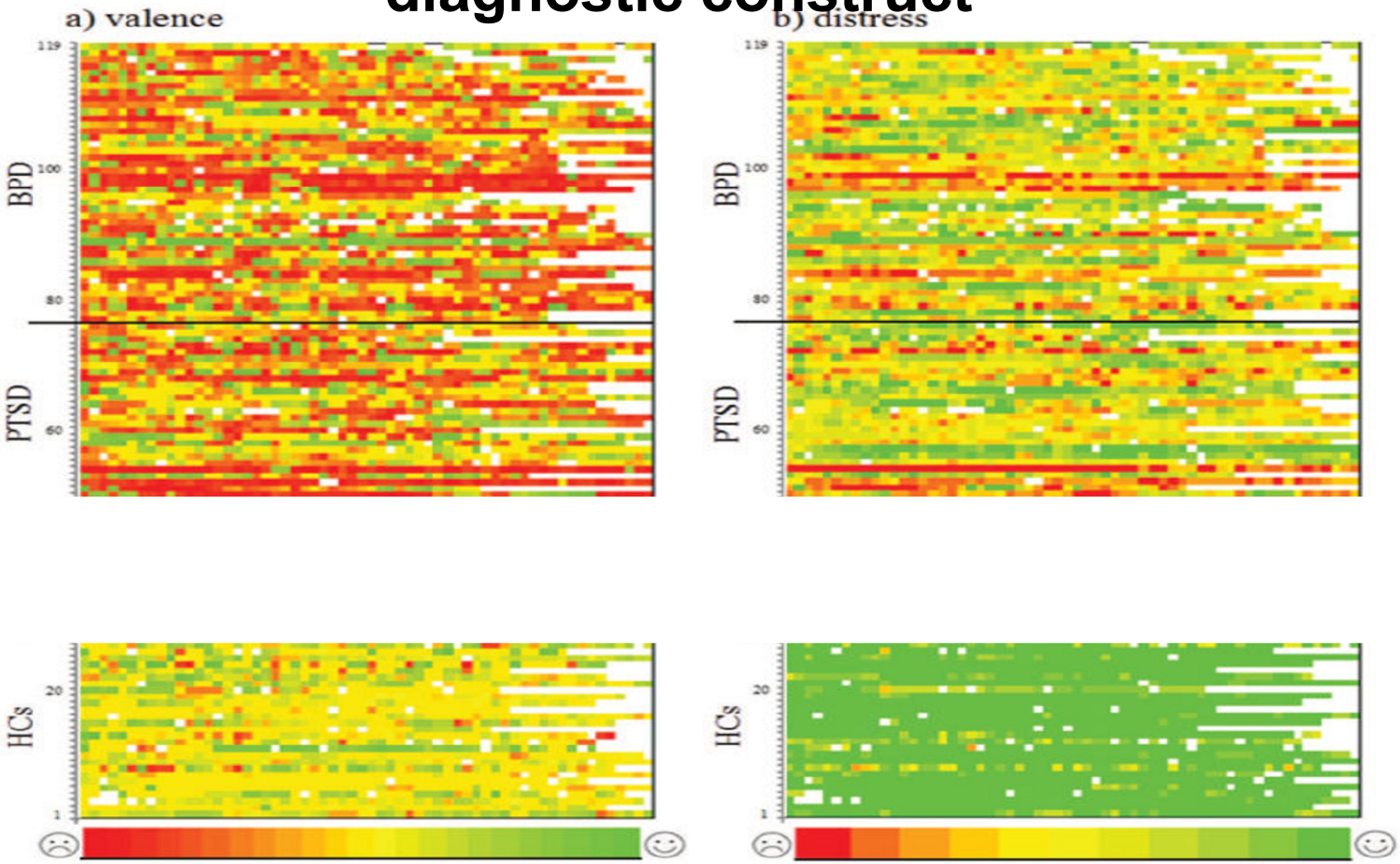

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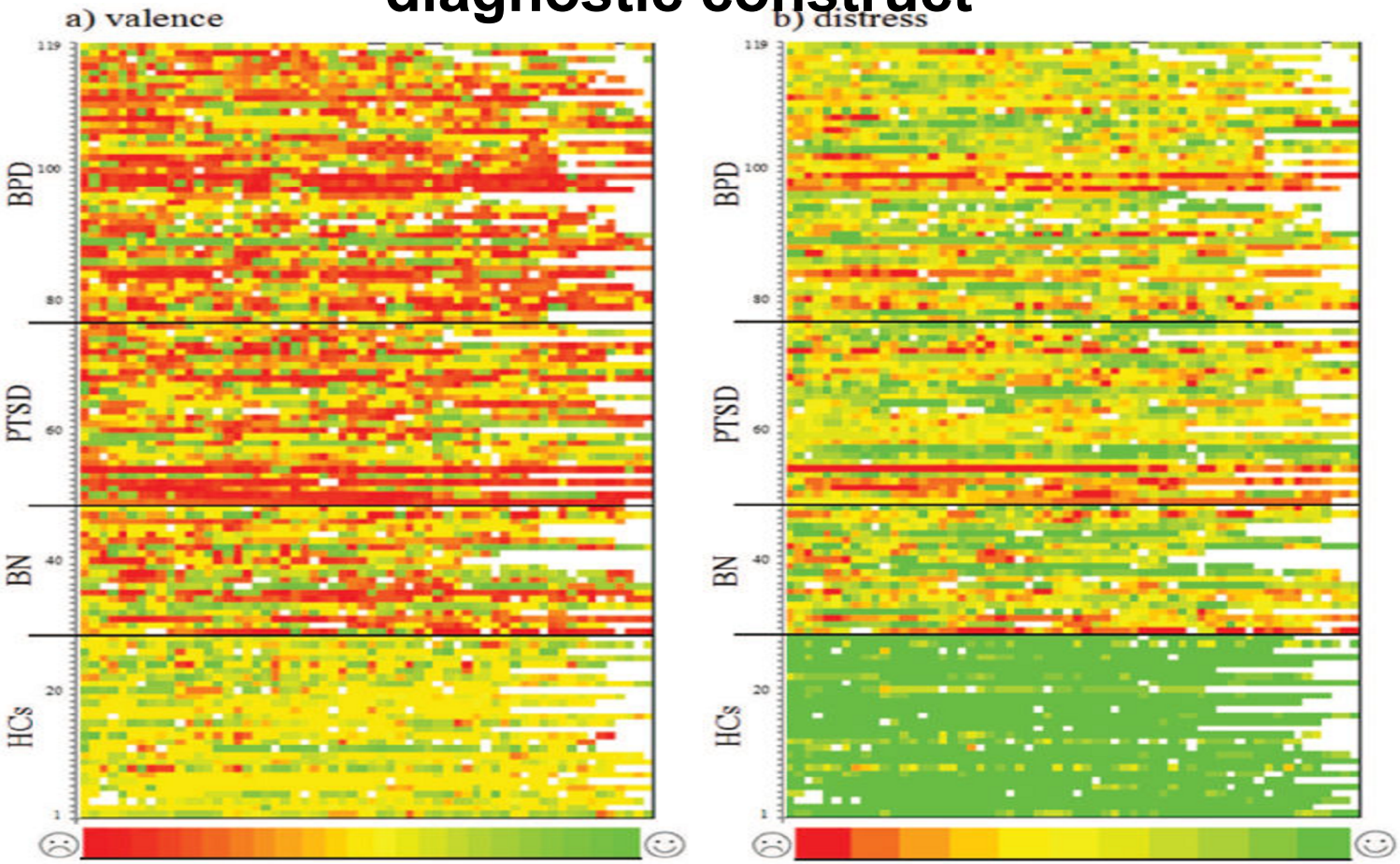

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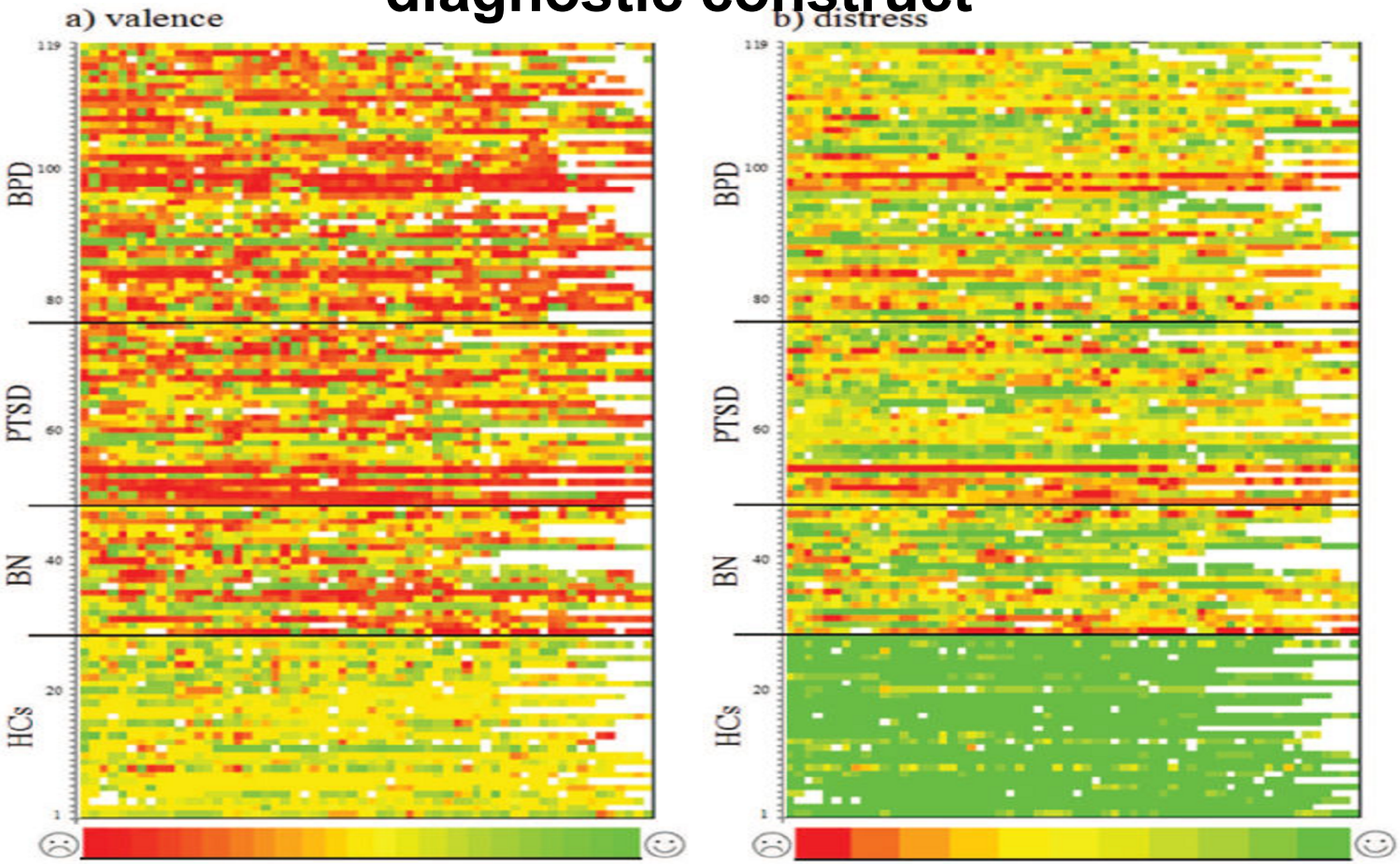

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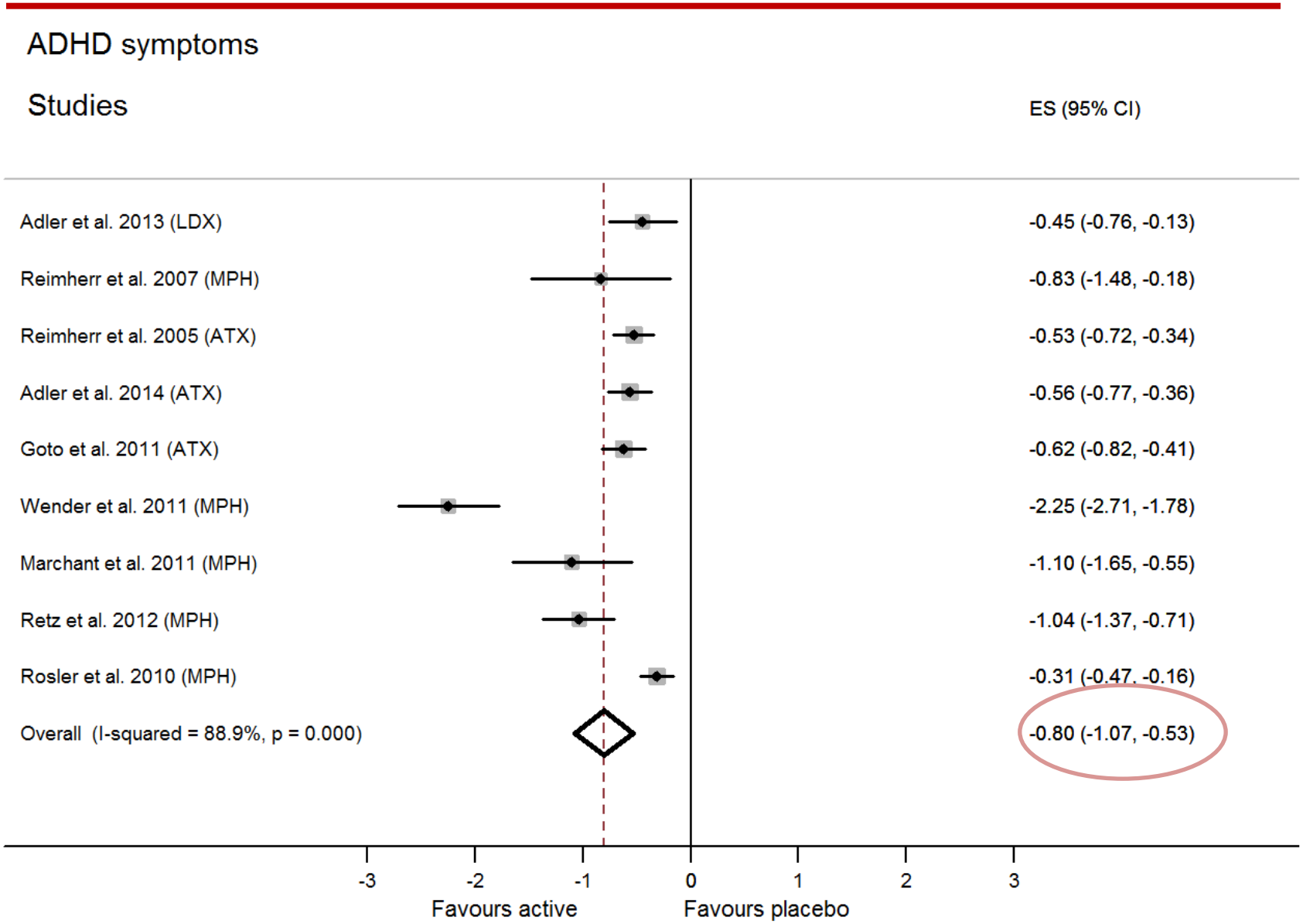
Wender-Reimherr Adult ADHD Diagnostic Scale (WRAADS)

Emotional Dysregulation Items

Affective lability	Temper control	Emotional over-reactivity
Mood fluctuations	Irritability	Overwhelmed
Dysphoric periods	Temper outbursts	Emotional reactivity
Boredom	Lack of control	Impairment
Overstimulation		

Results


ADHD symptoms
Studies
ES (95% CI)
Adler et al. 2013 (LDX)
-0.45 (-0.76, -0.13)
Reimherr et al. 2007 (MPH)
-0.83 (-1.48, -0.18)
Reimherr et al. 2005 (ATX)
-0.53 (-0.72, -0.34)
Adler et al. 2014 (ATX)
-0.56 (-0.77, -0.36)
Goto et al. 2011 (ATX)
-0.62 (-0.82, -0.41)
Wender et al. 2011 (MPH)
-2.25 (-2.71, -1.78)
Marchant et al. 2011 (MPH)
-1.10 (-1.65, -0.55)
Retz et al. 2012 (MPH)
-1.04 (-1.37, -0.71)
Rosler et al. 2010 (MPH)
-0.31 (-0.47, -0.16)
Overall (I-squared = 88.9%, p = 0.000)
-0.80 (-1.07, -0.53)
-3
-2
-1
0
1
2
3
Favours active
Favours placebo

Subgroup analyses

Sub-analyses domain	Studies	SMD[a]	95% CI
Stimulants on ED	**1,2,6-9**	**-0.57**	**-0.80 to -0.34**
Atomoxetine on ED	**3-5**	**-0.21**	**-0.34 to -0.08**
Stimulants + WRAADDS-EDS	**2,6-9**	**-0.64**	**-0.91 to -0.36**
Atomoxetine + WRAADDS-EDS	**3**	**-0.32**	**-0.50 to -0.13**
Stimulants + BRIEF-A	**1**	**-0.38**	**-0.68 to -0.04**
Atomoxetine + BRIEF-A	**4,5**	**-0.15**	**-0.30 to 0.00**

[a] Negative SMD favours a treatment effect for the active medication (stimulants or Atomoxetine)

1= Adler et al., 2013; 2= Reimherr et al., 2007; 3= Reimherr et al., 2005; 4= Adler et al., 2014; 5= Goto et al., 2011; 6= Wender et al., 2011; 7= Marchant et al., 2011; 8= Retz et al., 2012; 9= Rösler et al., 2010

Treatment algorithm

Chronic mental health problem (inattention, hyperactivity, impulsivity, emotional dysregulation

Screen for ADHD

No ADHD

Establish alternative diagnosis and treat accordingly (e.g. Bipolar disorder, personality disorder/ODD, anxiety/depression, alcohol/drug abuse, severe mood dysregulation)

Yes ADHD

No comorbidity **or** comorbid personality disorder

Significant depression, bipolar disorder, other condition

** Drug treatment for ADHD (stimulants or atomoxetine)

Treat comorbid disorder first in most cases

Review and consider additional treatments: CBT, anger management, other medicatio

** In children consider non-drug intervention first, if mild to moderate impairment

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Common symptoms seen in adult ADHD

- **Emotional instability: irritability, anger, affective lability**
- **Sleep onset (initial) insomnia**
- **Feeling restless (agitated when severe)**
- **Talking excessively or tangentially (severe ADHD)**
- **Low self-esteem**
- **Concentration difficulties**
- **Distractibility**
- **Impulsivity**
- **Mind wandering and ceaseless mental activity**

Asherson P. et al. J. of Att. Dis. 2012; 16;20S-38S.

ADHD and co-occurring mental health problems

A. Symptoms of ADHD (mimicking other disorders)

B. Overlapping neurodevelopmental disorders, specific and general learning difficulties

C. Development of co-occurring mental health disorders

Asherson et al., Lancet Psychiatry, 2016, 3: 568-78

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Symptoms and impairments of ADHD that can mimic other disorders

- **Anxiety:** excessive mind wandering, worrying about performance deficits, feeling overwhelmed, feeling restless, avoidance of situations due to ADHD symptoms (e.g. waiting in queues, social situations requiring focused attention), and sleep problems linked to mental restlessness

Asherson et al., Lancet Psychiatry, 2016, 3: 568-78

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- **Personality disorder (e.g. borderline):** chronic trait-like psychopathology, behavioural problems, emotional instability, impulsive behaviour, poor social relationships

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- **Depression:** chronic low self-esteem unstable moods, impatience, irritability, poor concentration, sleep disturbance
- **Personality disorder (e.g. borderline):** chronic trait-like psychopathology, behavioural problems, emotional instability, impulsive behaviour, poor social relationships
- **Bipolar disorder:** Restlessness and overactivity, sleep disturbance, mood instability, ceaseless unfocused mental activity, distractibility

Asherson et al., Lancet Psychiatry, 2016, 3: 568-78

Increasing the specificity of ADHD symptoms

Attention <u>Dysregulation</u> Hyperactivity Disorder

ADHD symptoms are not core deficits

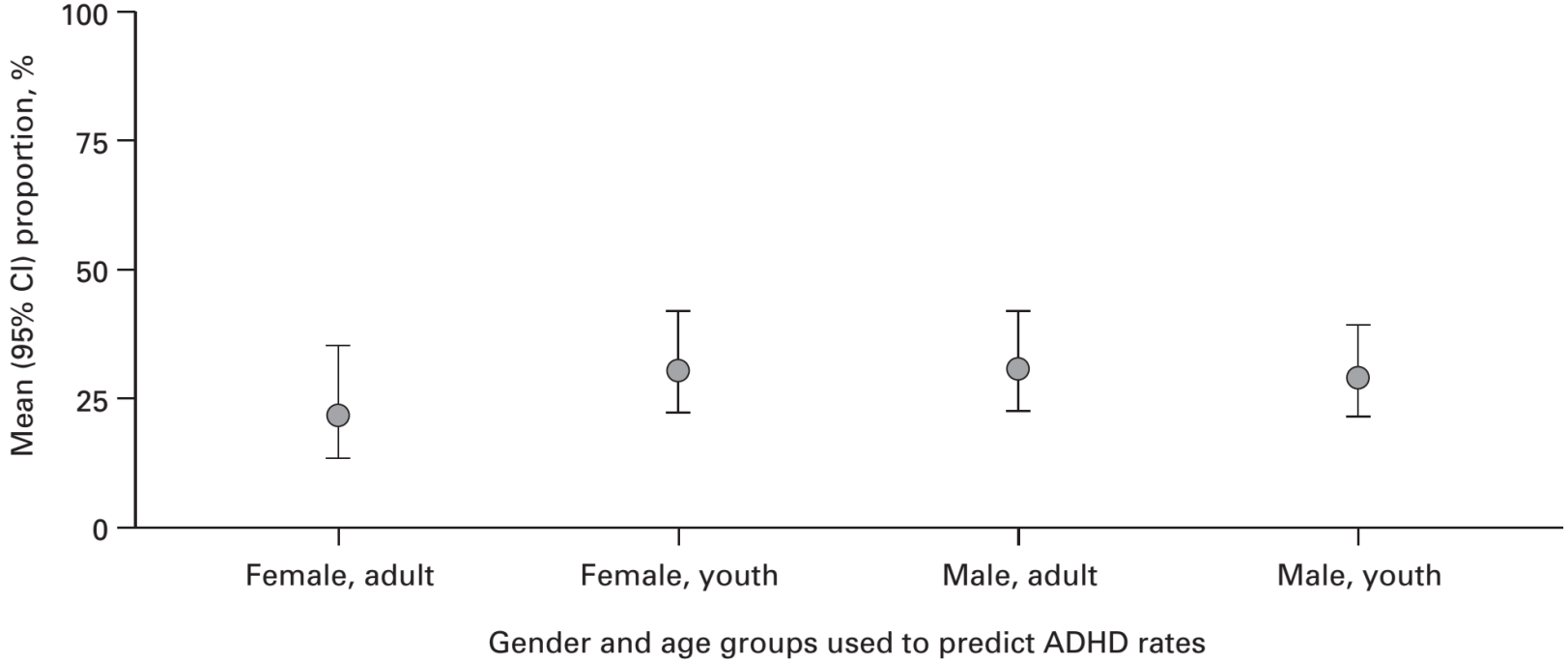
- Cluster of symptoms
- Hyper-focus
- Sensitivity to salience/reward
- Bored quickly and lose focus
- Spontaneous unconstrained mind wandering
- Impatience when waiting
- Happier when on the go doing something – irritable when there is nothing to do

Psychological Medicine, Page 1 of 12. © Cambridge University Press 2014
doi:10.1017/S0033291714000762

REVIEW ARTICLE

A meta-analysis of the prevalence of attention deficit hyperactivity disorder in incarcerated populations

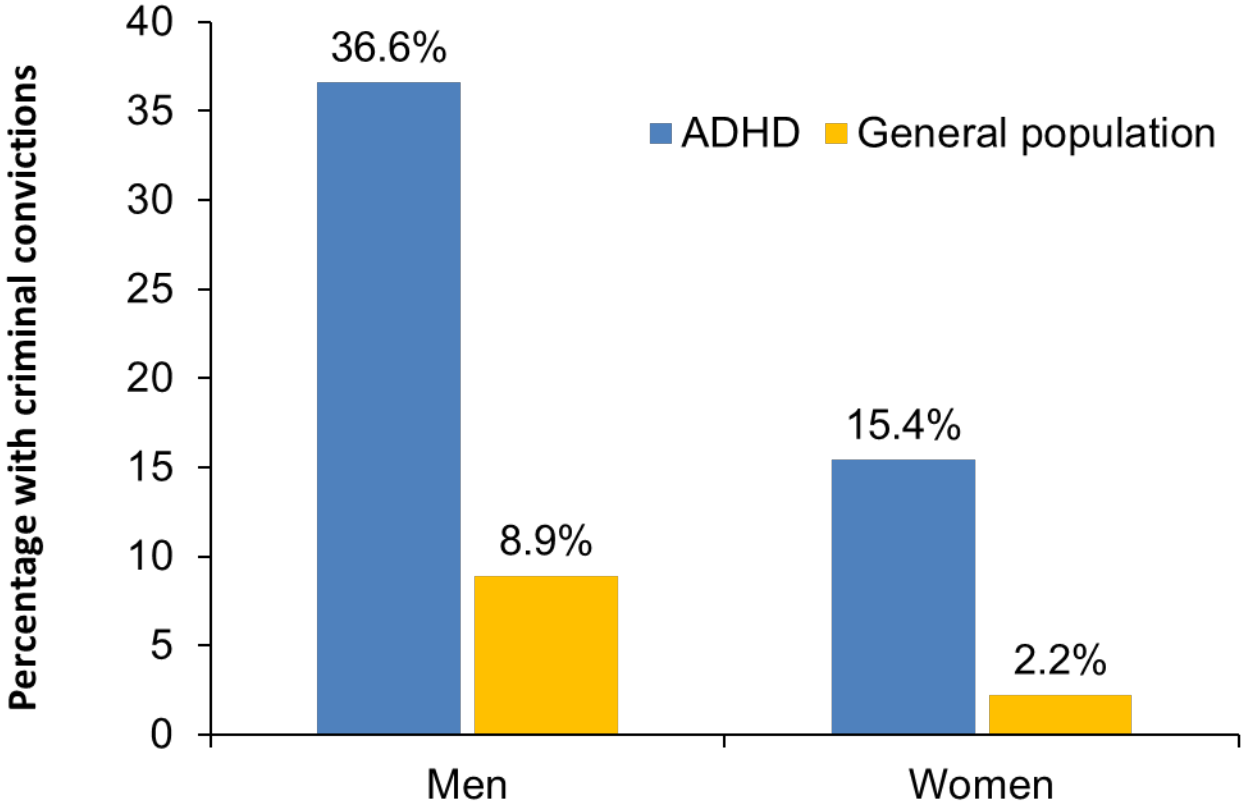
S. Young[1,2]*, D. Moss[3], O. Sedgwick[4], M. Fridman[5] and P. Hodgkins[6]



Estimated prevalence = 25.5%

Impact of adult ADHD on criminality

Proportion of Swedish adults with criminal convictions over a 4-year period (Jan 1, 2006 to Dec 31, 2009)



Lichenstein P, et al. *N Engl J Med*. 2012;367:2006-14.

Medication for ADHD and criminality: observational Swedish database analysis

Hazard ratio for conviction for any crime during ADHD medication (2006–2009) vs. non-medication periods

Treatment	Men (n = 16,087) Hazard ratio (95% CI)
All medications	0.68 (0.63–0.73)
Stimulants	0.66 (0.61–0.71)
Atomoxetine	0.76 (0.63–0.91)
SSRI medication	1.04 (0.93–1.17)

- Crimes occurred less often during medication periods:
  - men 32% reduction
  - women 41% reduction

Lichenstein P, et al. *N Engl J Med*. 2012;367:2006-14.

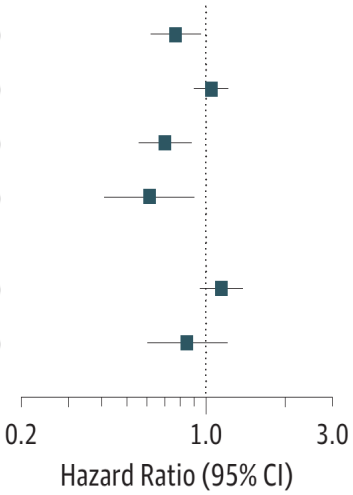
JAMA | Original Investigation

Association Between Prescription of Major Psychotropic Medications and Violent Reoffending After Prison Release

Zheng Chang, PhD; Paul Lichtenstein, PhD; Niklas Långström, MD; Henrik Larsson, PhD; Seena Fazel, MD

Figure 1. Between-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release

	Medicated Periods			Nonmedicated Periods				
Medication	Individuals, No.	Person-Years	Violent Reoffenses, No.	Individuals, No.	Person-Years	Violent Reoffenses, No.	Risk Difference in No. of Violent Reoffenses/ 1000 Person-Years (95% CI)	Hazard Ratio (95% CI)
Antipsychotics	2063	1590	100	2727	10941	1036	-21.7 (-35.9 to -3.7)	0.77 (0.62 to 0.96)
Antidepressants	5597	3831	224	7297	30786	2018	2.6 (-6.5 to 13.7)	1.04 (0.90 to 1.21)
Psychostimulants	1197	1647	94	1343	4538	513	-33.9 (-49.7 to -13.5)	0.70 (0.56 to 0.88)
Drugs used in addictive disorders	2063	1164	46	3009	15565	1098	-27.5 (-41.6 to -7.0)	0.61 (0.41 to 0.90)
Antiepileptics	2213	1972	152	2703	10659	798	10.4 (-3.7 to 28.4)	1.14 (0.95 to 1.38)
Adrenergic inhalants[a]	2370	1289	38	2844	12892	580	-6.7 (-18.0 to 9.0)	0.85 (0.60 to 1.20)



Association Between Prescription of Major Psychotropic Medications and Violent Reoffending After Prison Release

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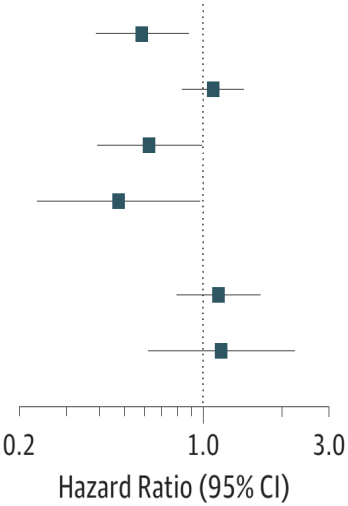
Figure 2. Within-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release

Medication	Medicated Periods			Nonmedicated Periods			Risk Difference in No. of Violent Reoffenses/ 1000 Person-Years (95% CI)	Hazard Ratio (95% CI)
	Individuals, No.	Person-Years	Violent Reoffenses, No.	Individuals, No.	Person-Years	Violent Reoffenses, No.		
Antipsychotics	2085	1596	100	2767	11 026	1044	-39.7 (-57.7 to -11.3)	0.58 (0.39 to 0.88)
Antidepressants	5660	3846	224	7421	31 135	2038	5.9 (-11.1 to 28.1)	1.09 (0.83 to 1.43)
Psychostimulants	1202	1648	94	1352	4553	513	-42.8 (-67.6 to -2.2)	0.62 (0.40 to 0.98)
Drugs used in addictive disorders	2077	1168	46	3055	15 725	1103	-36.4 (-54.0 to -2.1)	0.48 (0.23 to 0.97)
Antiepileptics	2235	1976	152	2736	10 750	800	10.4 (-15.6 to 48.3)	1.14 (0.79 to 1.65)
Adrenergic inhalants[a]	2387	1291	38	2878	12 992	586	-7.6 (-17.1 to 55.4)	1.17 (0.62 to 2.23)



The CIAO Project

Professor Philip Asherson- Chief Investigator

Clare Evans- Research Worker/Project Coordinator

Co-investigators: Susan Young, Andrew Forester, Declan Murphy

HM PRISON SERVICE

South London and Maudsley NHS
NHS Foundation Trust

MRC Social Genetic and Developmental Psychiatry

CIAO: A pilot study of Concerta XL In Adult Offenders with ADHD

Aim: To evaluate the effectiveness of Concerta XL in reducing levels of aggression, increasing engagement with educational activities and reducing symptoms of ADHD, in young male offenders with ADHD

Method: 12-week open label study of 100 offenders with ADHD, with 6-month extension.

Drug: Concerta XL 18 – 90 mg titrated to optimal effect

Participants: Male prisoners aged 18-30 (most 18-24)

Site: The trial will take place at HMPYOI Isis.

The CIAO study

- Screened
- N = 1,922

- Screen positive
- N = 473 (25%)

- Diagnostic assessment
- 398 (84%)

- •Positive assessments
- •N = 278 (77%)

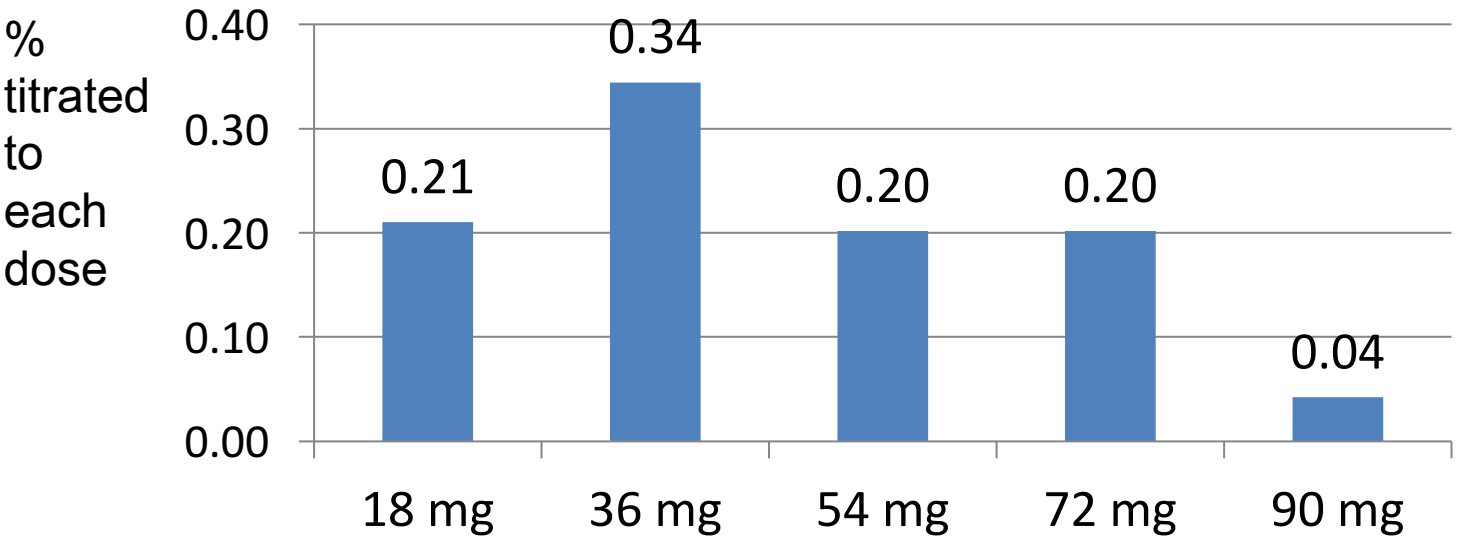
- **19.3%** of prison population met DSM-5 ADHD criteria
- **121** (40%) treated with OROS-MPH

CIAO: final report 2015

Abuse potential and diversion

- Stimulants are controlled drugs with risk for diversion – but diversion in the community usually by college students
- Psychiatric drugs diverted within prisons (e.g. Mirtazapine, Quetiapine)
- Limited abuse potential unless insufflated or injected
- Preparations that are difficult to abuse: Concerta XL and Elvanse

Limited drug seeking behaviour observed in Concerta trial



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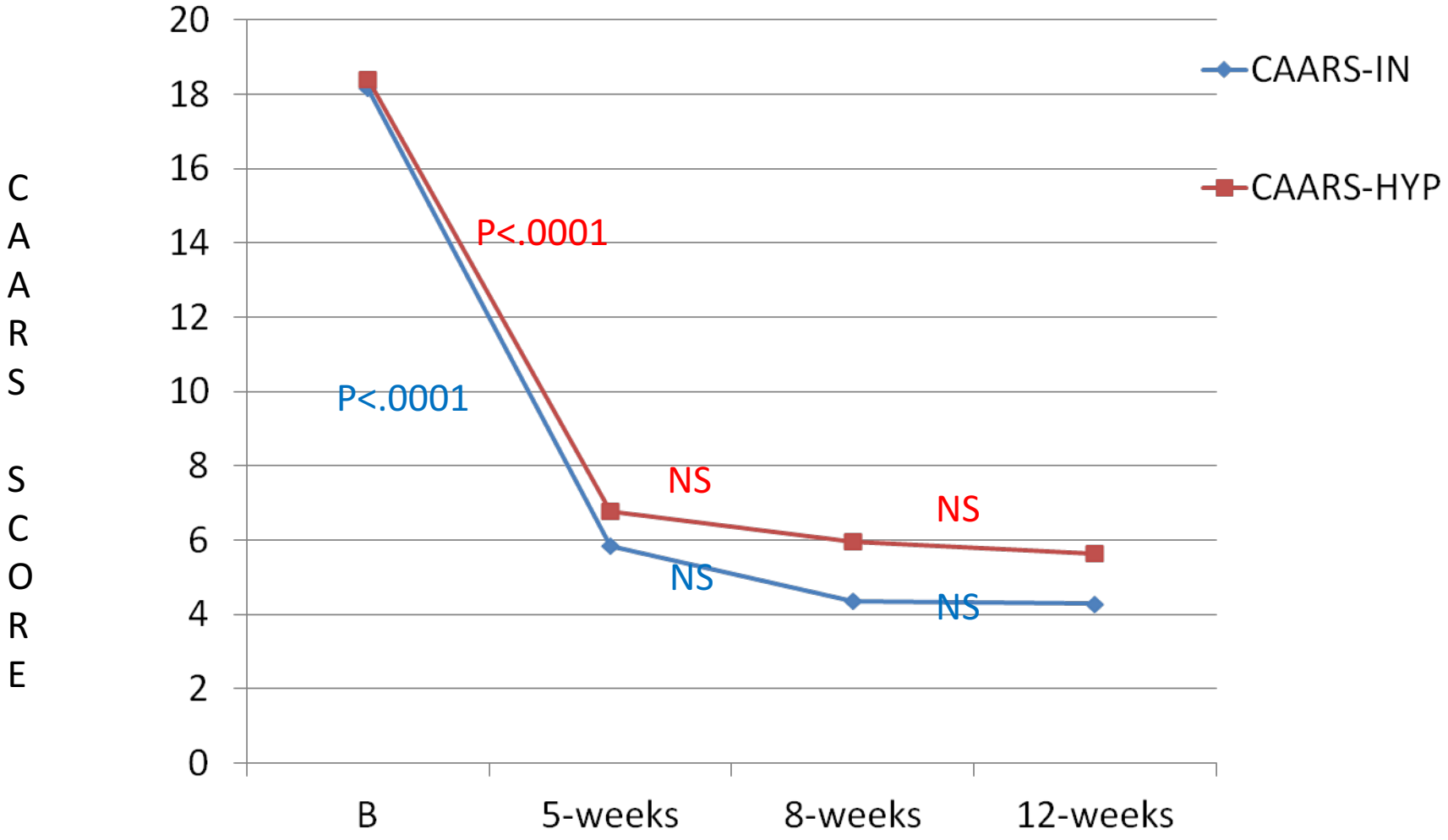
CIAO: Observer rated ADHD symptoms scores



CIAO: final report 2015

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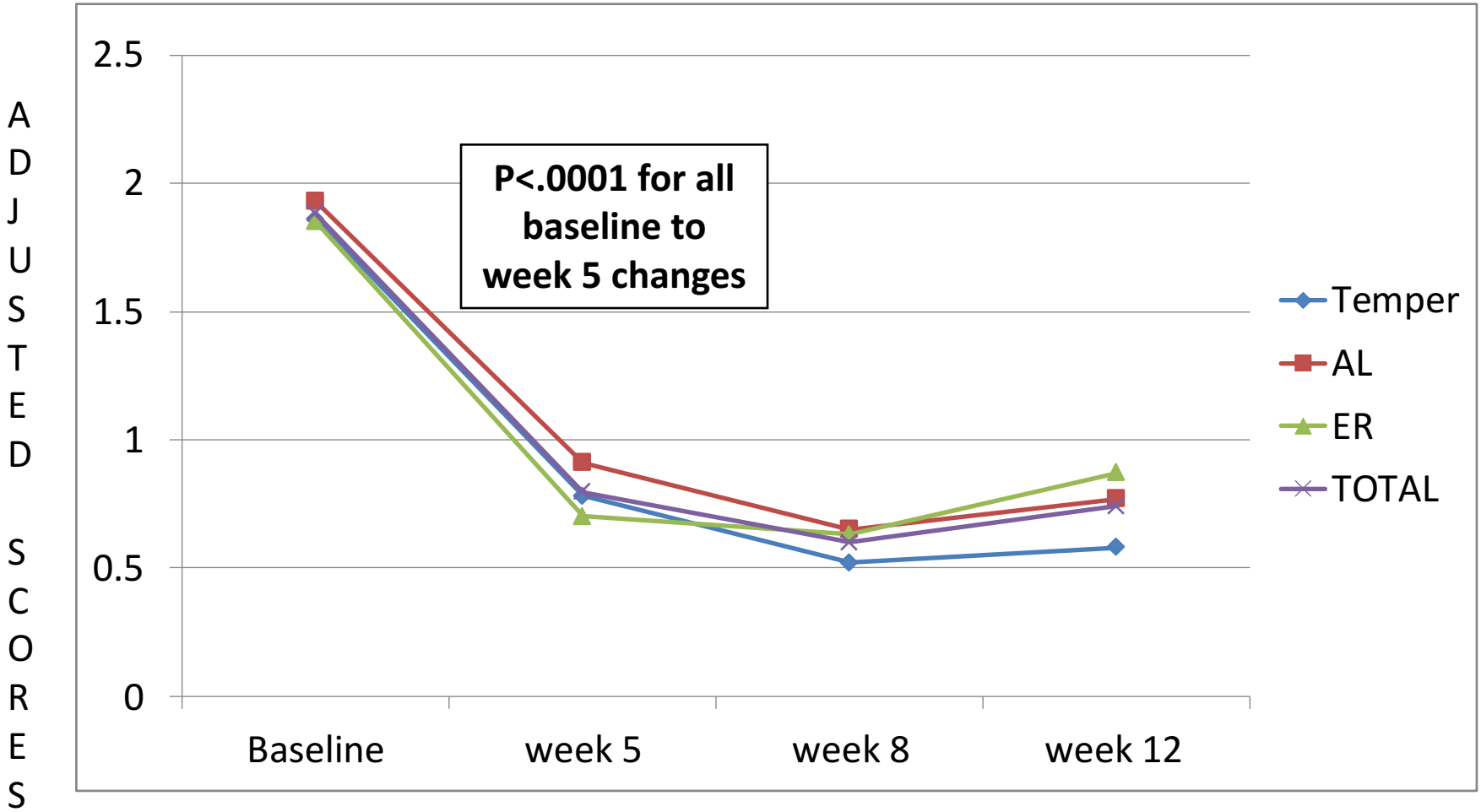
Investigator rated emotional instability

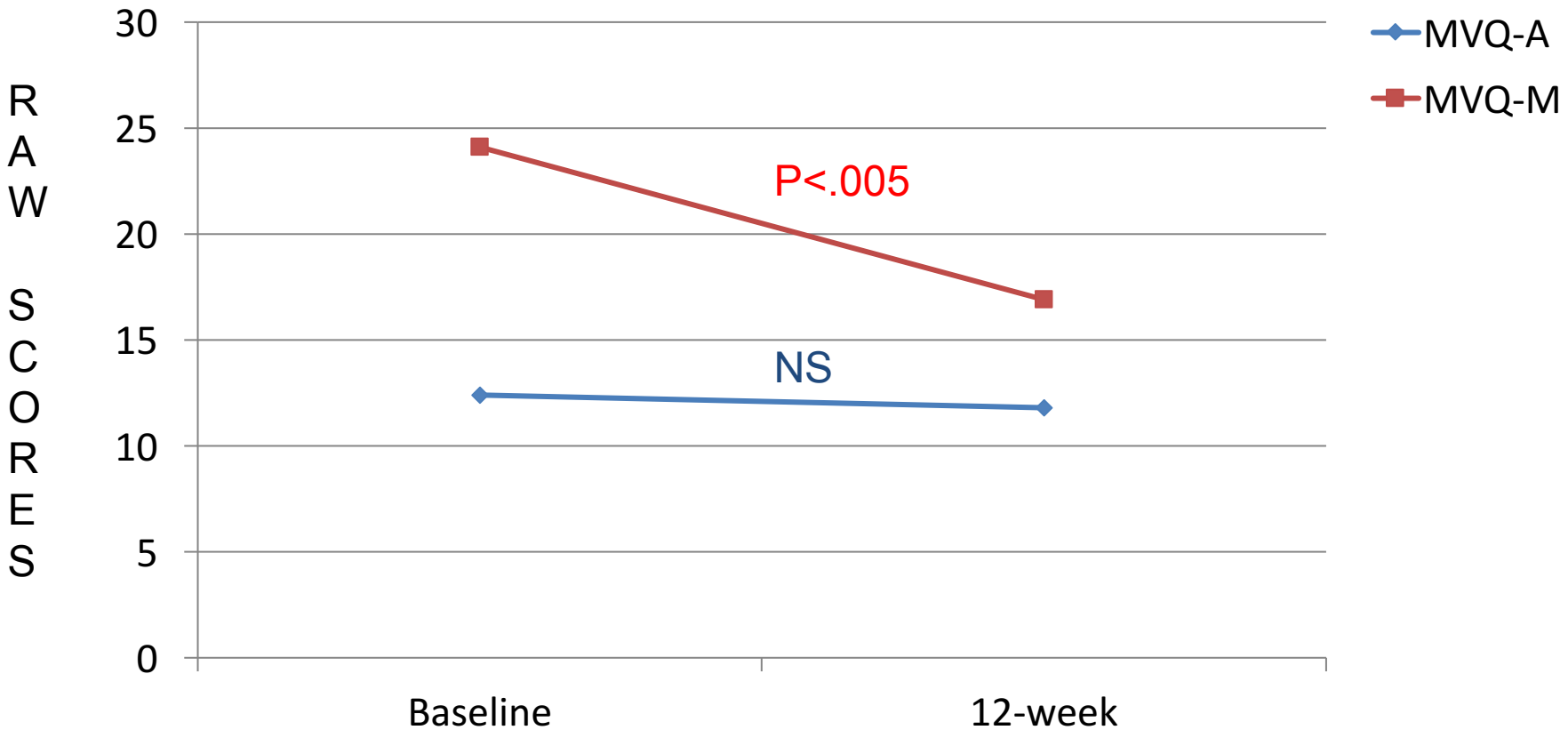
Temper control; Mood lability (AL); Emotional Reactivity (ER)



CIAO: final report 2015

UKAAN
UK ADULT ADHD NETWORK

CIAO: Maudsley Violence Questionnaire



CIAO: final report 2015

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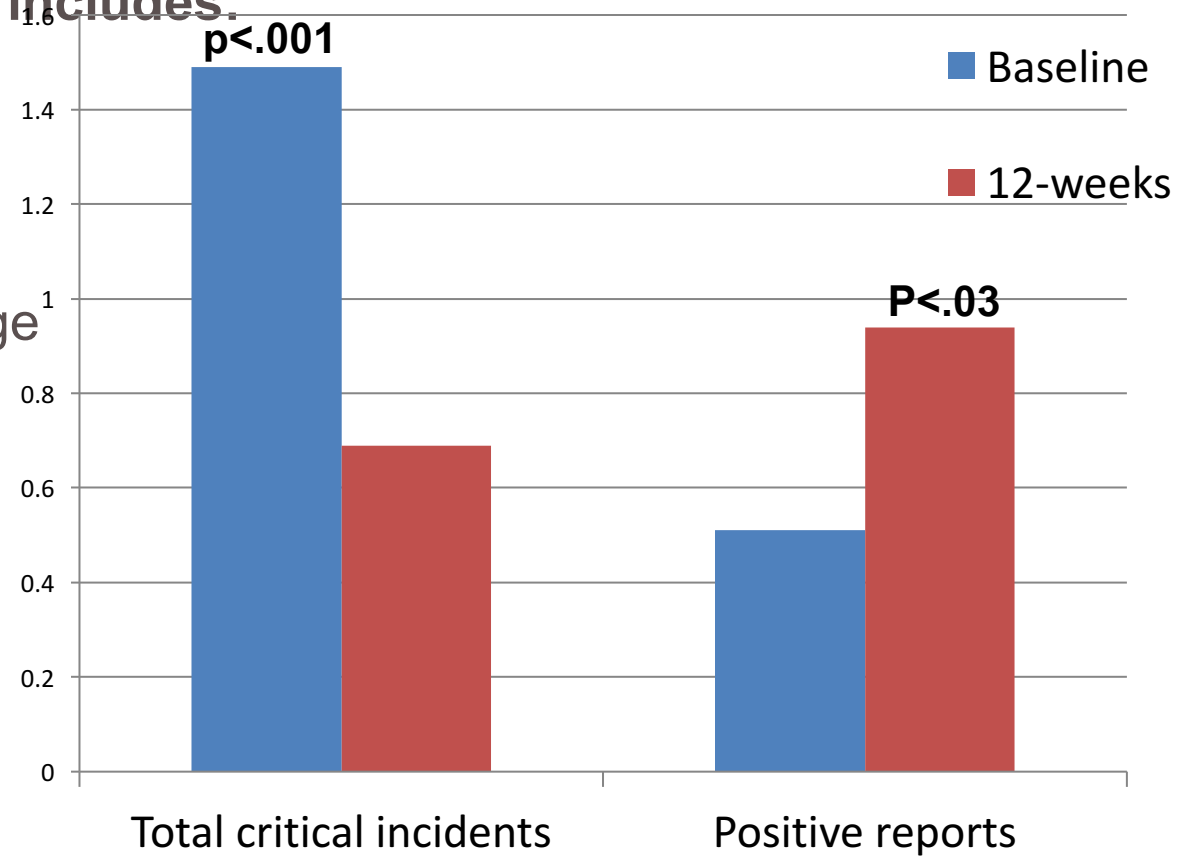
Preliminary report: Number of critical incidents recorded in prison records:

- **Total critical incidents includes:**
  - Total serious assault
  - Total assault
  - Total fights
  - Total property damage
  - Total self harm
  - Total taking drugs
  - Total disobey



CIAO: Based on data 8th December 2013

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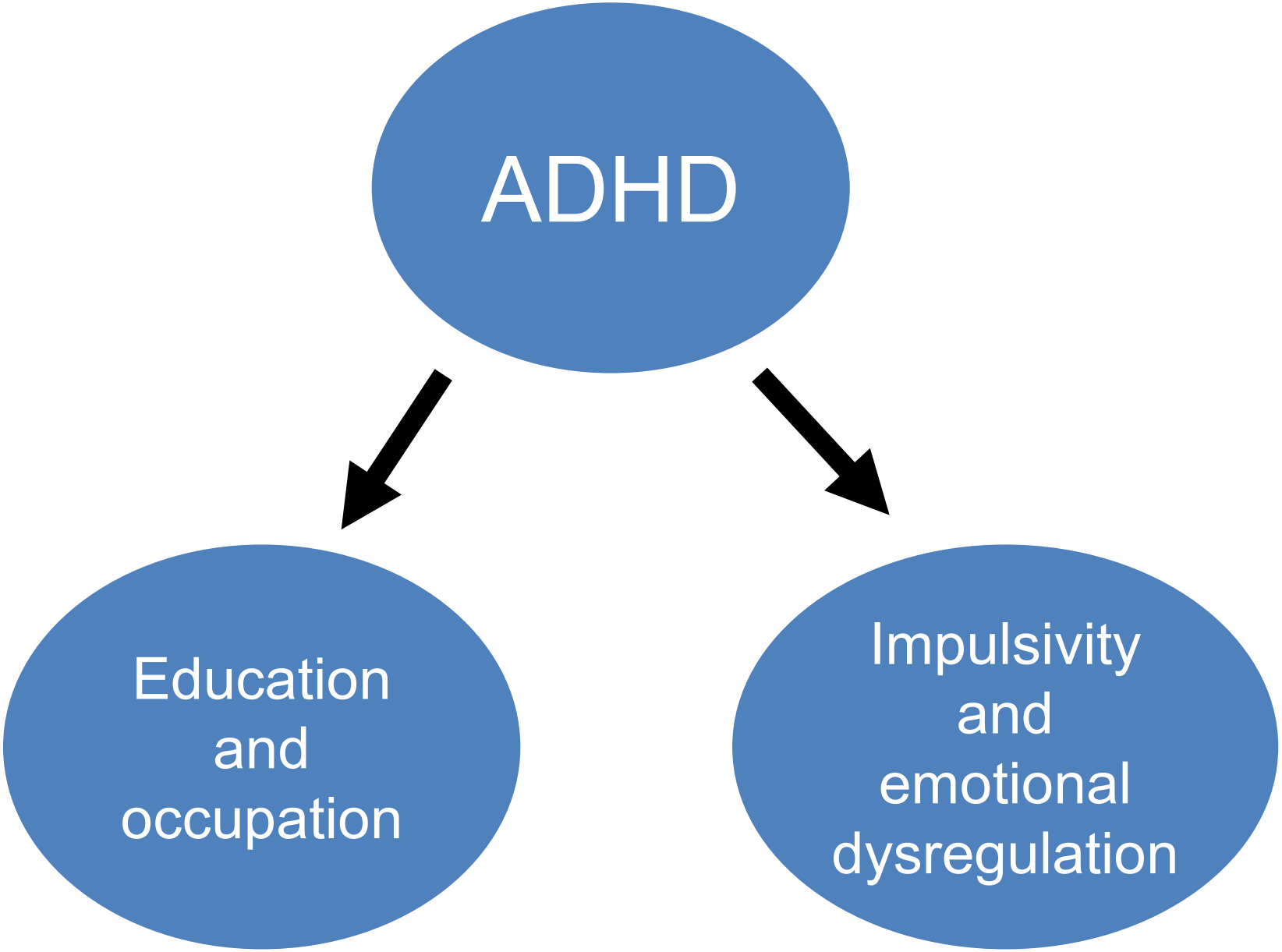
Summary of significant effect sizes (Cohen's d)

Outcome	Cohen's d ITT	Cohen's d pp
Investigator rated (I) or self-rated scales (S)		
Inattention (I)	2.27	3.00
Hyperactivity-impulsivity (I)	2.11	2.78
Emotional dysregulation (I)	1.49	1.71
Affective lability (S)	1.19	1.65
MVQ-Machismo (MVQ) (S)	0.60	0.98
MVQ-Acceptance of violence (S)	0.37	0.40
Prison records of behaviour		
Sum of adjudications	0.30	0.53
Percentage attended activities	0.07 (ns)	0.34
Sum of positive IEPs	0.25	0.36
Days in enhanced regime	0.14	0.19

CIAO: final report 2015


ADHD
Education and occupation
Impulsivity and emotional dysregulation

Feedback from Prison Inspectorate

- **Outside unbiased perspective**
- **Inspectors highlighted the CIAO project:**

"All prisoners were offered screening for attention deficit hyperactivity disorder (ADHD) through the specialist Concerta (an ADHD treatment) in adult offenders (CIAO) trial…Some prisoners on the CIAO programme to whom we spoke were experiencing some stability of behaviour for the first time in their lives."

The HMIP report recommended continued support beyond the prison:

"There should be efforts to ensure the continued prescribing of medication and ongoing specialist support for prisoners started on the CIAO trial following their release"

Her Majesty's Inspectorate of Prisons' report carried out in February of 2014
http://www.imb.org.uk/wp-content/uploads/2015/01/isis-2013.pdf

Thanks!

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Jonna Kuntsi
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Ruth Cooper
Andrew Forrester
Declan Murphy
Susan Young
Stefanos Maltezos and the SLAM Maudsley ADHD clinic team

Funders
- European Union (F7)
- Medical research council
- Wellcome Trust
- National Institute of Health Research
- Action Medical Research
- National Institute of Mental Health
- Janssen-Cilag
- Social Genetic and Developmental Psychiatry
- Institute of Psychiatry Psychology and Neuroscience
- King’s College London